Prediction of cancer mutation states using multiple data modalities reveals the utility and consistency of gene expression and DNA methylation

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Background

Research questions:
• Which -omics type captures the functional signatures of cancer mutations most effectively? Is this dependent on the gene(s) that are mutated?
• Does combining multiple -omics types improve detection?

Framing as a prediction problem:
We want to predict cancer mutation presence or absence using -omics data in the TCGA Pan-Cancer Atlas: gene expression, DNA methylation, reverse phase protein array (RPPA), microRNA, somatic mutational signatures.

Approach

• Cancer gene set from Vogelstein et al. 20132: ~85 cancer-related genes
• Elastic net logistic regression
• 2 replicates (random seeds) x 4-fold CV, stratified by cancer type
• Compare classifiers against baseline with permuted labels, and compare directly between data types

Results

On aggregate over the Vogelstein et al. gene set, gene expression is a slightly more effective predictor than the methylation arrays (Illumina 27K/450K merged and Illumina 450K).

Looking at performance for individual genes, however, most genes do not significantly differ between data types (data points around origin).

When we compare all data types using all cancer genes, the expression and DNA methylation datasets significantly outperform the remaining data types.

For the remaining data types, on the individual gene level, gene expression generally provides better performance (genes/points in the top left).

We also built multi-omics models by concatenating combinations of the expression and methylation datasets. For each data type, we used the top 5000 principal components as predictive features.

Using six pan-cancer driver genes as targets, none of the multi-omics models significantly outperformed the best-performing single-omics model.

Relevant Links

Data and code availability:
https://github.com/greenelab/mpmp
Draft of manuscript (currently in-progress using Manubot3):
https://greenelab.github.io/mpmp-manuscript/
Link to this poster:

References


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